REMARKS

The application has been amended to delete David B. Agus and Howard I. Scher under 37 C.F.R. §1.48(b) as a result of amendment of claim 1 and cancellation of claims in the prior amendment. As a result of these amendments, the contributions of Agus and Scher are no longer claimed in the application.

Claim 1 has been amended to recite that the antibody which binds ErbB2 blocks ligand activation more effectively than monoclonal antibody 4D5. This amendment is supported in the specification at page 13, line 37 to page 14 line 3 (see also page 14, lines 4-5 and Example 4 found on page 50). Claim 31 has been added which reproduces the language of amended claim 1, but recites androgen independent prostate cancer as supported on page 38, line 36. Claim 4 is amended to refer to an antibody which "blocks formation of an ErbB hetero-oligomer" as supported on page 14, line 5, and claim 28 refers to an antibody which binds to an ErbB2 epitope bound by monoclonal antibody 2C4 as supported on page 16, lines 7-12; these amendments do not alter the scope of the other claims in the application. The recitation of "the biological characteristics of monoclonal antibody 2C4" is removed from claim 22.

I. Particularity and Distinctiveness of the Claims

The Examiner has rejected claims 4, 5, and 22-30 under 35 U.S.C. §112, second paragraph, contending that claims 4, 22, and 28 are indefinite for reciting "having the biological characteristics of monoclonal antibody 2C4." The Examiner explains that this may encompass any number of characteristics that have not been described in the specification.

In response, the applicants have amended claims 4, 22 and 28 to recite particular characteristics of the antibodies for use in the invention. While particular characteristics are set forth I the claims, such antibodies may have other properties as would be well-known. The specification describes a number of such biological activities, such as binding ErbB2 antigen (specification at page 13, lines 28-36), blocking ligand activation (specification at page 13, line 37 to page 14, line 12) and specifically blocking HRG activation of an ErbB2 hetero-oligomer comprising ErbB2 and ErbB3 or ErbB4; blocking EGF, TGF-α, HB-EGF, epiregulin and/or amphiregulin activation of an ErbB receptor comprising EGFR and ErbB2; blocking EGF, TGF-α and/or HRG mediated activation of MAPK; and/or binding the same epitope in the

extracellular domain of ErbB2 that is bound by 2C4, e.g., blocking binding of monoclonal antibody 2C4 to ErbB2 (specification at page 14, line 15-20).

That other biological activities of 2C4 may exist is irrelevant, as the monoclonal antibody is deposited and thus available for testing those biological activities. The existence of such biological activities would be well known to one of ordinary skill in the art and consequently the term "having the biological characteristics of monoclonal antibody 2C4" is sufficiently well defined as to fully meet the requirements to particularly point out and to distinctly claim the subject matter of the invention under 35 USC § 112, Second paragraph.

Notwithstanding this, without acquiescing in the rejection, the offending language is removed from claim 22 and claims 4 and 28 are amended herein to recite particular activities of the antibody used in the methods in order to expedite prosecution.

In view of the foregoing, Applicants respectfully submit that the Examiner's rejection is obviated and should be withdrawn.

II. Enablement of the Claimed Methods

The Examiner has maintained the rejection of claims 1-9 under 35 U.S.C. §112, first paragraph, contending that the specification, while being enabling for a method of treating prostate cancer in mammals by administering the anti-ErbB2 antibody 2C4, does not reasonably provide enablement for method of treating a human having prostate cancer or androgen dependent prostate cancer when the method comprises administering any ErbB2 antibody.

Applicants respectfully traverse this rejection. The present invention is directed to identification of a particular class of antibodies that bind to the ErbB2 receptor and are capable of effectively providing treatment for prostate cancer, particular androgen independent prostate cancer. As the Examiner has recognized, the ability of antibodies like 4D5 and MDX-210 to bind ErbB2 and provide a therapy for prostate cancer is known. What was previously not known, and is the subject of the present discovery, are the characteristics of ErbB2 antibodies that provide more effective treatment of prostate cancer, especially androgen independent prostate cancer. In addition to 2C4, antibody 7F3 is exemplified as being useful for treating androgen independent prostate cancer in conjunction with TAXOL® (specification, page 56, lines 5-10). The present inventor has discovered an antibody with the ability to block ligand

activation of an ErbB2 receptor to a greater degree than antibody 4D5 (which the Examiner's own references show has been used in treatment of prostate cancer) is especially effective in therapy of prostate cancer, particularly androgen independent prostate cancer. And as pointed in the prior amendment filed August 13, 2002 (see pages 6-8, which are incorporated herein by reference), there can be no doubt that antibodies having the characteristics as claimed in claim 1 are fully enabled by the specification. There is also no doubt that such antibodies, as has been discovered for antibodies in general, can be administered to subjects suffering from prostate cancer.

Applicant has established that antibodies having these characteristics are particularly effective for treating prostate cancer, particularly androgen independent prostate cancer. The Examiner has not provided any grounds to cast doubt on these statements in the specification or to establish a question of enablement of these elements of the claimed invention. However, the Examiner bears the burden to provide evidence sufficiently to refute the affirmative statements made in the specification. See MPEP §2164.04; *In re Wright*, 27 U.S.P.Q2d 1510, 1513 (Fed. Cir. 1993).[1]

The Examiner has failed refute any of the arguments for enablement provided in the amendment filed August 13, 2002. Applicant thus refers to the Examiner's explanation for the enablement rejection in the Office Action dated February 13, 2002 to establish lack of enablement. At the filing date of 1999, the antibody art was well developed and mature such that the skilled artisan could generate antibodies to a well characterized antigen like the ErbB2 antigen of the present application. Applicant has support in the specification and recites in the claims the binding characteristics and activities that render the antibodies effective for the claimed method of treatment. Accordingly, the Examiner's argument with respect to selection of antibodies that fall within the scope of the claim lacks merit; such antibodies are enabled and fully within the ability of the ordinary artisan without undue experimentation. In view of the filing date and the present disclosure, generation of ErbB2 antibodies and testing them for the presently claimed biological activity would not have involved undue experimentation. Generating antibodies is well established in the art and has been for 30 years. Identifying

[1] It continues to be unclear why the Examiner persists in rejecting claims 2, 4, and 5 which the Examiner concedes are enabled.

biological activity of such antibodies as presently claimed is fully disclosed in the specification (see e.g., pages 13-14, 32-35 and the Examples). In a case such as this, the scope of enablement is quite broad because the level of unpredictability is extremely narrow.

The Examiner points out that there can be from a million to ten billion possible antibodies. Again, it is has been well established that selecting antibodies with specific binding activities from this million to ten billion is within the level of ordinary skill in the art (arguably, it is well within the level of the skill of an undergraduate biology major). Further testing for the claimed biological activity is also routine, certainly within the skill of a trained laboratory technician, graduate student, or post doctoral associate (and likely within the level of skill of a bright undergraduate). Were the mere selection of a biological molecule having a desired activity from millions or billions of choices to constitute undue experimentation, there is little or no work in biology that would be enabled. Virtually every experimental process in biology involves selecting a desired product (e.g., a hybridoma, clone, transformed cell, etc.) from millions of alternatives. Indeed, the great power of molecular biology, biochemistry, and cell biology lies in the ability to select the one in a million to one in a billion desired product from among all the others. See *Hybritech Inc. v. Monoclonal Antibodies Inc.*, 802 F.2d 1367, 231 USPQ 81 (Fed Cir. 1986) (methods of making and screening monoclonal antibodies were known to those skilled in the art); and *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (1988) (immunoassay methods using a generic class of antibodies was enabled despite deposit of one specific antibody because those skilled in the art could produce and screen other hybridomas).

The Examiner points out that the inventor should be allowed to dominate future patentable inventions of others where those inventions are based in some ways on his teachings (Office Action of 2/13/03, page 5). There is no doubt about the enabling extent of the teachings in this case, and any use of an ErbB2-binding antibody as claimed to treat prostate cancer is based on the teachings of the specification.

In view of the foregoing remarks, Applicants respectfully submit that the specification fully enables the claims as amended and the rejection should be withdrawn.

III. Novelty and Non-Obviousness of the Claimed Invention

A. Rejections Under 35 U.S.C. §102

The Examiner has rejected claims 1 and 8 under 35 U.S.C. §102(e). The Examiner contends that the rejected claims are anticipated by Greene et al., U.S. Patent 5,842,311 ("Greene"), published October 20, 1998, or Arakawa et al., U.S. Patent 5,783,186 ("Arakawa"), published July 21, 1998.

The Examiner contends that Greene teaches a method of treating the activated p185 oncogene, found in prostate adenocarcinoma, by administration of an antibody. The Examiner contends that Arakawa teaches a method of treating a patient by using monoclonal antibodies which bind to ErbB2 to treat mammalian cancer tumors which express HER2 on their surface.

Applicants respectfully traverse this rejection and reconsideration is respectfully requested.

Claim 1 recites that the antibody blocks ligand activation of an ErbB receptor more effectively than monoclonal antibody 4D5 (*e.g.*, Herceptin®). We can look to the specification to define the meaning of this term. The specification states that an "antibody which 'blocks' ligand activation of an ErbB receptor is one which reduces or prevents such activation as hereinabove defined, wherein the antibody is able to block ligand activation of the ErbB receptor substantially more effectively than monoclonal antibody 4D5, *e.g.* about as effectively as monoclonal antibodies 7F3 or 2C4 or Fab fragments thereof and preferably about as effectively as monoclonal antibody 2C4 or a Fab fragment thereof." (Specification, page 13, line 37 to page 14, line 4). The antibodies disclosed in Greene do not block ligand activation and certainly not to a greater extent than 4D5. Greene discloses that the mechanism of the cytotoxic effect is unknown, but that it is likely due to down-modulation, and complement mediated lysis, as evidenced by experimental results (Greene, col. 4, lines 14-15; col. 8, lines 32-36; col. 10, lines 47-63). Similarly, Arakawa merely discloses that the monoclonal antibody described therein induces apoptosis through a phosphorylation-dependent mechanism (col. 3, lines 1-6; Example 5). There is no disclosure in Arakawa that the monoclonal antibody blocks ligand activation of ErbB2 in the manner required by the teachings of the instant invention. Therefore, the invention

is not anticipated by either Greene or Arakawa because the claims as amended require the therapeutic antibody block ligand activation of the ErbB receptor more effectively than previously known therapeutic anti-ErbB monoclonal antibodies, *i.e.*, Herceptin®.

The Examiner has rejected claims 1, 6, and 8-9 as anticipated by Curnow, Cancer Immunology Immunotherapy, Vol. 45., pages 210-215, 1997. The Examiner contends that Curnow teaches a method of treating a human patient by administering an antibody which binds ErbB2 and blocks activation of an ErbB receptor.

Applicants respectfully traverse this rejection and reconsideration is respectfully requested.

Curnow discloses a bispecific antibody that binds CD64 antigen and HER2/neu, designated MDX-H210. Such an antibody brings a CD64-positive effector cell in proximity of a HER2/neu bearing cell. Thus, the Curnow antibody mediates its therapeutic activity through a cell-mediated immune response mechanism, not by direct effects on ErbB2. Curnow does not disclose or even suggest that MDX-H210 blocks ligand activation of an ErbB2 receptor, much less that it does so more effectively than 4D5. To the contrary, Curnow proposes that MDX-210 (non-humanized anti-HER2/neu) directs phagocytosis of tumor cells by antigen presenting cells, resulting in the presentation of tumor antigens and induction of a humoral response, and that this same activity has been suggested for humanized MDX-H210 (Curnow, page 213, column 1, bottom). Thus, Curnow does not teach an antibody that blocks ligand activation of an ErbB receptor more effectively than monoclonal antibody 4D5 for treating prostate cancer; the reference teaches something quite different. In view of the preceding, Curnow cannot anticipate the claims of the instant application. Withdrawal of this rejection is respectfully requested.

B. Rejections Under 35 U.S.C. §103

The Examiner has rejected claims 1 and 8 as unpatentable over Hudziak et al., U.S. Patent 5,725,826 ("Hudziak"), issued March 10, 1998 in view of Ching (the full name of the author is Karen Zhi Ching), Dissertation Abstracts, Vol. 55, No. 11, page 4738-B, May 1995 ("Ching"). The Examiner contends that Hudziak teaches that the HER2 oncogene has been found active in numerous cancers, and further provides a method of using monoclonal antibodies which bind to ErbB2 to treat mammalian cancer tumors which express HER2 on their surfaces (Office

Action, p. 13). The Examiner contends that Ching teaches that prostate cancer overexpresses HER2. The Examiner further contends that Murphy teaches that the term "prostate cancer" generally refers to androgen dependent prostate cancer.

Applicants respectfully traverse this rejection and reconsideration is respectfully requested.

The preferred monoclonal antibody 4D5 in Hudziak inhibits the growth of breast tumor line SKBR3 (col. 18, lines 13-18). However, the amended claims are directed to use of antibodies that block ligand activation of an ErbB more effectively than 4D5. Hudziak does not specifically mention the desirability of this property for treating prostate cancer. Ching does not supply the missing teaching.

Ching does not disclose specific antibodies, nor does Ching disclose the characteristics of ErbB2 antibodies that would be useful for treating prostate cancer. The *in vitro* experiments reported in Ching provide no bases for predicting an *in vivo* effect (absent the teaching of the invention), or even a comparison of relative activities. As evidenced by the discussion of Arakawa and Greene above, alternative mechanisms can result in tumor growth inhibition.

The data presented in the specification of the claimed invention support that 2C4 blocks EGF, TGF-α, and heregulin-mediated activation of MAP kinase (MAPK) to a greater extent than 4D5 (Example 4, page 50). Example 1 (page 45) demonstrates that 2C4 inhibits proliferation of the HER2 over-expressing cell line MDA-MB-175 with constitutively phosphorylated ErbB2 to a greater extent than 4D5. The superior results elicited by 2C4 are due to its biological characteristic of "blocking ligand activation" as outlined in the specification (page 13, line 37 to page 14, line 12) by, *e.g.*, preventing association of ErbB2 with either EGFR or ErbB3 (page 50, lines 24-26).

The relevant test for obviousness requires three basic factual inquiries: the scope and content of the prior art are to be determined; the differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the art resolved. *Graham v. Deere*, 383 U.S. 1, 17 (1966). Applicants respectfully submit that the scope of the prior art falls well short of suggesting, much less teaching the claimed invention. In particular, the

primary reference, Hudziak, specifically teaches monoclonal antibody 4D5, which the claims have been amended to explicitly exclude. Ching does not supply the missing teaching. Accordingly, this rejection fails to establish *prima facie* obviousness and should be withdrawn.

The relevant inquiry for obviousness is whether the prior art suggests the invention and whether the prior art provides one of ordinary skill in the art with a reasonable expectation of success. *In re O'Farrell*, 7 USPQ2d 1673 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art and not in the Applicant's disclosure. *In re Vaeck*, 20 USPQ 2d 1438 (Fed. Cir. 1991). The references cited by the Examiner provide neither the suggestion nor the reasonable expectation of success. Accordingly, this rejection should be withdrawn.

The Examiner has rejected claims 1 and 8 under 35 U.S.C. §103(a) as unpatentable over Ching, May 1995, in view of Baselga et al., Oncology, Suppl. 2, March 1997 ("Baselga I"), or Baselga et al., Journal of Clinical Oncology, Vol. 14, No. 3, pages 737-744, March 1996 ("Baselga II"). The Examiner contends that Baselga I and Baselga II teach a method of treating a human patient whose diagnosis includes the overexpression of ErbB2 receptor by administering an effective amount of anti-ErbB2 antibody which binds the extracellular domain. As discussed above, the Examiner contends that Ching teaches a method of treating prostate cancer by administering an antibody which binds ErbB2 and blocks activation of an ErbB receptor.

Applicants respectfully traverse this rejection and reconsideration is respectfully requested.

Baselga I discusses the use of anti-HER2 antibodies to treat breast malignancies. Baselga I discloses that 4D5 is a potent antibody for this purpose. Baselga I also discloses that recombinant humanized 4D5 (Herceptin®) is more potent than murine 4D5 as it is "much more efficient in supporting antibody-dependent cellular cytotoxicity" (page 46, col 1). Baselga I does not disclose that humanized or murine 4D5 HER2 blocks ligand-mediated activation to a greater degree than itself, as required by the claimed invention as amended.

Baselga II discloses results of Phase II studies with Herceptin ® in the treatment of breast cancer. On page 742, col. 1, line17-19, to col. 2, line 1-17 Baselga II discusses several

possible mechanisms that could explain the observed results, including HER2 receptor down-regulation, agonistic induction of a "death-inducing" signaling pathway, and induction of ADCC. Blocking ligand-mediated activation is not disclosed or suggested.

In view of the above, absent specific teaching in Ching of a comparative ability of an anti-ErbB to inhibit ligand activation more than monoclonal antibody 4D5, much less the advantage of such a characteristic to treating prostate cancer, and a similar lack of disclosure in Baselga I, and Baselga II, the combination of references fails to suggest the invention. In fact, Baselga I and Baselga II only fairly teach administration of a 4D5 anti-HER2 antibody, which is explicitly excluded by the claims as amended. Correctly applying the *Graham* factors, it is readily apparent that the Examiner has not established *prima facie* obviousness. Accordingly, this rejection should be withdrawn.

The Examiner has rejected claims 1-4 and 6-9 under 35 U.S.C. §103(a) as obvious over Greene, or Arakawa, or Curnow, or Hudziak, or Zhi (sic, Ching) or Baselga I, or Baselga II, in further view of Fendly et al., Cancer Research, Vol. 50, pages 1550-1558, March 1, 1990 ("Fendly"), or Shepard et al., Journal of Clinical Immunology, Vol. 11, No.9, pages 117-126, 1991 ("Shepard"), all in view of Schlom, Molecular Foundations of Oncology, pages 95-134 ("Schlom"). The teachings of Greene, Arakawa, Curnow, Hudziak, Ching, Baselga I, and Baselga II have been discussed above. None of these references teach or suggest using an antibody that blocks ligand activation of ErbB2 more than monoclonal antibody 4D5-indeed, Hudziak, Baselga I, and Baselga II specifically teach using a 4D5 antibody.

The Examiner contends that Fendly and Shepard teach that the monoclonal antibody 2C4 selectively binds HER2, and that it would have been obvious for one of ordinary skill in the art to use the 2C4 antibodies of Fendly and Shepard to practice the methods of Greene and Arakawa. The Examiner asserts that blocking ligand activation would be an inherent characteristic of the Fendly and Shepard antibodies.

The Examiner contends that Schlom describes the various known antibody modifications, including Fabs, and that these fragments provide a therapeutic advantage of reducing the host anti-monoclonal antibody response. Thus, the Examiner alleges that it would have been obvious to use the Fab's of Schlom to practice the methods of Greene, or Arakawa or Curnow or Hudziak or Zhi or Baselga I or Baselga II or Fendly or Shephard, and one would have

been motivated to do so because the Fab's reduce the host anti-antibody response.

Applicants respectfully traverse this rejection and reconsideration is respectfully requested.

Fendly teaches that monoclonal antibody 2C4 is intermediate in its ability to immunoprecipitate HER2, and that two other anti-EGFR monoclonal antibodies (5G3 and 6C5) blocked ligand binding to EGFR (*not* to its oncogenic counterpart HER2/ErbB2). Fendly does not teach or suggest that (1) 2C4 (or any antibody) blocks ligand activation of an ErbB receptor, as recited in the claims herein, or (2) that such a property renders the antibody particularly useful for treating prostate cancer, especially androgen independent prostate cancer. That teaching comes from the instant specification.

Shepard teaches that the mechanism by which 2C4 inhibits growth of breast tumor cells is not understood, but that it likely is due to cross-reactivity with another receptor on the cell surface (page 120, col. 2). Shepard further explains that a "critical property" of an anti-$p185^{HER2}$ antibody with potential for therapy is its *lack* of cross-reactivity with other receptors (page 119, col. 2). Like Fendly, Shepard does not teach that 2C4 blocks ligand activation of an ErbB2 receptor as reacted in the claims, or that such a property renders the antibody especially useful for treating prostate cancer.

Fendly describes production of a panel of 10 anti-$p185^{HER2}$ monoclonal antibodies, without indicating which, if any, are potentially therapeutic (Fendly does note that prior publications reported that several anti-$p185^{HER2}$ monoclonal antibodies inhibit breast cell line proliferation *in vitro*, citing, Hudziak *et al.*, Mol. Cell Biol. 1989, 9:1165-1172). In particular, in contrast to the present invention as claimed, Fendly does not describe the characteristics of an anti-ErbB2 antibody that render it more effective for treating prostate cancer, especially androgen-independent prostate cancer: that the antibody blocks ligand activation of the ErbB2 receptor more effectively than monoclonal antibody 4D5. Moreover, Shepard promotes antibody 4D5, one of over 100 monoclonals tested, for treating p185 HER2 over-expressing tumor cells. Shepard further teaches away from using a cross-reactive antibody, like 2C4, in therapy (Shepard, pps. 119-120). These two references, taken for what they fairly teach, when combined with the primary references, lead one to employ 4D5 to treat prostate cancer. Indeed, Shepard reports that 4D5 was most effective against another cancer besides

breast carcinoma, as it was also effective against an ovarian tumor line (Shepard, p. 120). No other conclusion is fairly available from this combination of references. In this respect, Fendly and Shepard add nothing to the teachings of Hudziak, Baselga I, and Baselga II. But the claimed invention recites that the antibody blocks ligand activation of an ErbB receptor more effectively than monoclonal antibody 4D5, thus distinguishing the claims from the very subject matter that the references lead one of ordinary skill in the art to pursue.

Certainly there is no reasonable expectation from the references of record that therapy with antibodies that bind $p185^{HER2}$, and not pursued in deference to antibody 4D5, would be effective for treating prostate cancer. The only basis for such a conclusion is from the instant disclosure, in which case the rejection relies on hindsight gained from the instant disclosure to support this rejection. Such a basis for rejecting the claims is improper. The Examiner cannot rely on hindsight to arrive at a determination of obviousness. *In re Fritch*, 23 U.S.P.Q.2d 1780, 1784 (Fed. Cir. 1992). The Court of Appeals for the Federal Circuit has stated that "selective hindsight is no more applicable to the design of experiments than it is to the combination of prior art teachings. There must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the Applicant's disclosure" [*Interconnect Planning Corporation v. Fed.*, 227 U.S.P.Q. 543, 551 (Fed. Cir. 1985)]. *In re Dow Chemical Co.*, 5 U.S.P.Q.2d 1529, 1532 (Fed. Cir. 1988).

It bears noting at this point that 4D5 antibodies like Herceptin® may be useful cancer therapeutics, including prostate cancer. However, the present invention is distinct from such teachings because the antibody must block ligand activation of an ErbB receptor more effectively than 4D5. Since it is quite clear that 4D5 cannot meet this limitation (the antibody cannot be more effective than itself), the claimed invention is unobvious. Withdrawal of this rejection is respectfully requested.

With respect to Curnow, this reference teaches a bi-specific antibody capable of bringing a CD64-positive effector cell in contact with HER2 target cell. As explained above, the mechanism of action for such a bispecific antibody is distinct from the presently claimed biological function of the antibody. Furthermore, since Shepard clearly identifies 4D5 as the best therapeutic candidate, it is clear that the criteria for activity according to Curnow do not define a useful therapeutic antibody, as claimed. In short, there is no incentive to combine these

references, and the references, if combined, do not teach the claimed invention. They teach away from it, which is the paradigm of a lack of a reasonable expectation of success. Generally, when a reference teaches away from the claimed invention, the requisite teaching to establish *prima facie* obviousness is absent, thus precluding a conclusion of unpatentability. See *In re Bell*, 26 USPQ2d 1529 (Fed. Cir. 1993). The Court of Appeals for the Federal Circuit has stated:

> A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent form the path that was taken by the applicant [citation omitted].

In re Gurley, 27 F.3d 551 (Fed. Cir. 1994). Therefore, withdrawal of this rejection is respectfully requested.

The Examiner contends that Schlom describes the various known antibody modifications, including Fab's and that these fragments provide a therapeutic advantage of reducing the host anti-monoclonal antibody response. Thus, the Examiner alleges that it would have been obvious to use the Fab's of Schlom to practice the methods of Greene, or Arakawa, or Curnow, or Hudziak, or Zhi, or Baselga I, or Baselga II, or Fendly, or Shephard, and one would have been motivated to do so because the Fab's reduce the host anti-antibody response.

Applicants respectfully traverse this rejection and reconsideration is respectfully requested. As pointed out above, none of the references taken alone or in combination describe using an antibody that binds an ErbB receptor and blocks ligand activation of an ErbB receptor more than antibody 4D5, to treat prostate cancer. If the references teach anything, it is to use a 4D5 antibody to treat prostate cancer. While this may very well be a useful prostate cancer treatment modality, since 4D5 cannot be more effective than 4D5 in blocking ligand activation of an ErbB receptor, the claimed invention distinguishes over all of the references in combination (noting, for the record, that some or all of the combinations are simply improper).

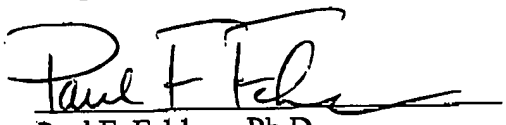
Schlom does not provide the missing teaching. The description of antibody fragments can hardly substitute for the teaching found in the specification: that an antibody having the claimed properties will be useful for treating prostate cancer. Therefore, in view of the above remarks and the legal principles of obviousness, withdrawal of this rejection is in order.

CONCLUSION

Applicant respectfully requests entry of the foregoing amendments and remarks into the file history of this application. All of the alleged grounds for unpatentability of the claims have been addressed by this response. Applicant earnestly solicits allowance of the application.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted,



Paul F. Fehlner, Ph.D.
Reg. No. 35,135
Attorney for Applicants

DARBY & DARBY, P.C.
Post Office Box 5257
New York, NY 10150-5257
Phone (212) 527-7700